Medicare Coverage Policies for New Medical Technologies

CENTERS FOR MEDICARE & MEDICAID SERVICES (CMS)
CENTER FOR CLINICAL STANDARDS & QUALITY
COVERAGE & ANALYSIS GROUP

Medicare Begins: 1965

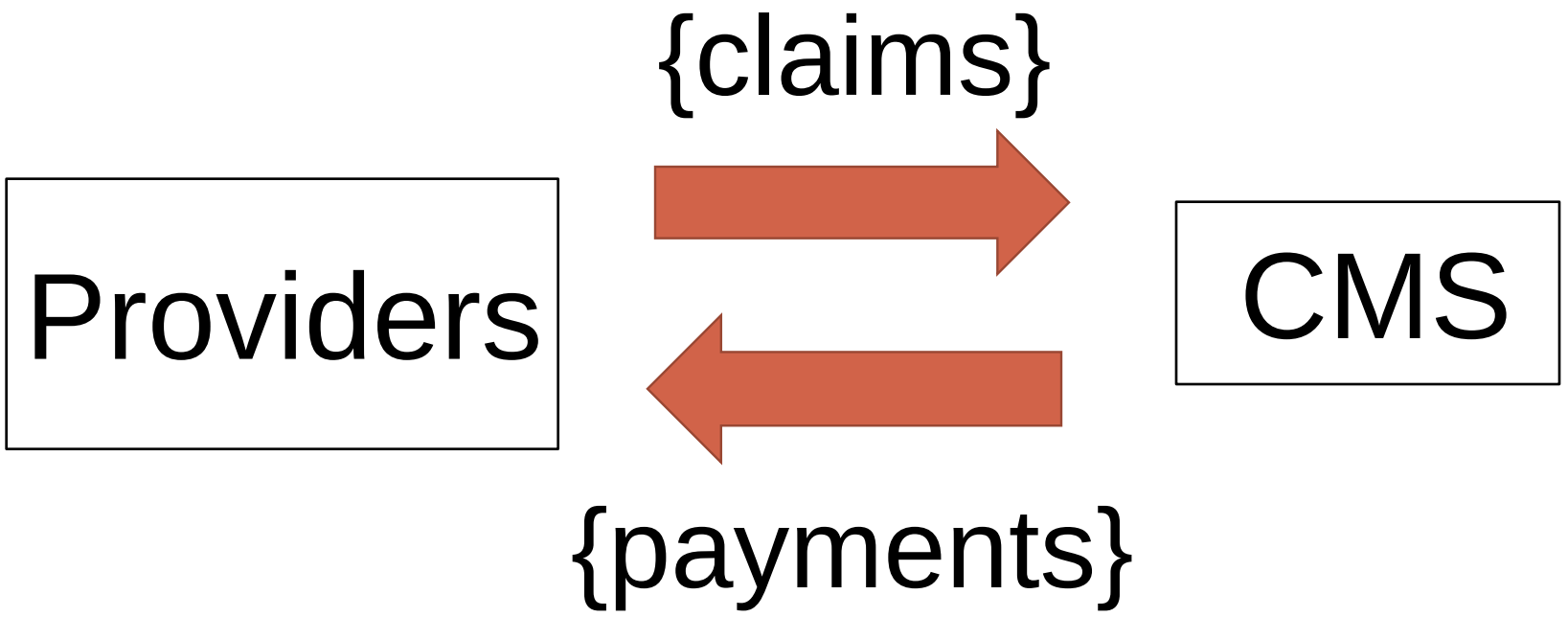
President Lyndon B. Johnson at the signing ceremony July 30, 1965, at the Truman Library in Independence, Missouri.

Source: CMS / ORDI

Principles of the Medicare Program

- Inaugural Address, 1949:
  - "This great Nation cannot afford to allow its citizens to suffer needlessly from the lack of proper medical care. **Our ultimate aim must be a comprehensive insurance system to protect all our people equally against insecurity and ill health**." - President Harry S. Truman
- Remarks to President Truman at the signing ceremony for Medicare, Independence, Mo., 1965:
  - “(T)hrough this new law, Mr. President, every citizen will be able, in his productive years when he is earning, to insure himself against the ravages of illness in his old age.” - President Lyndon B. Johnson

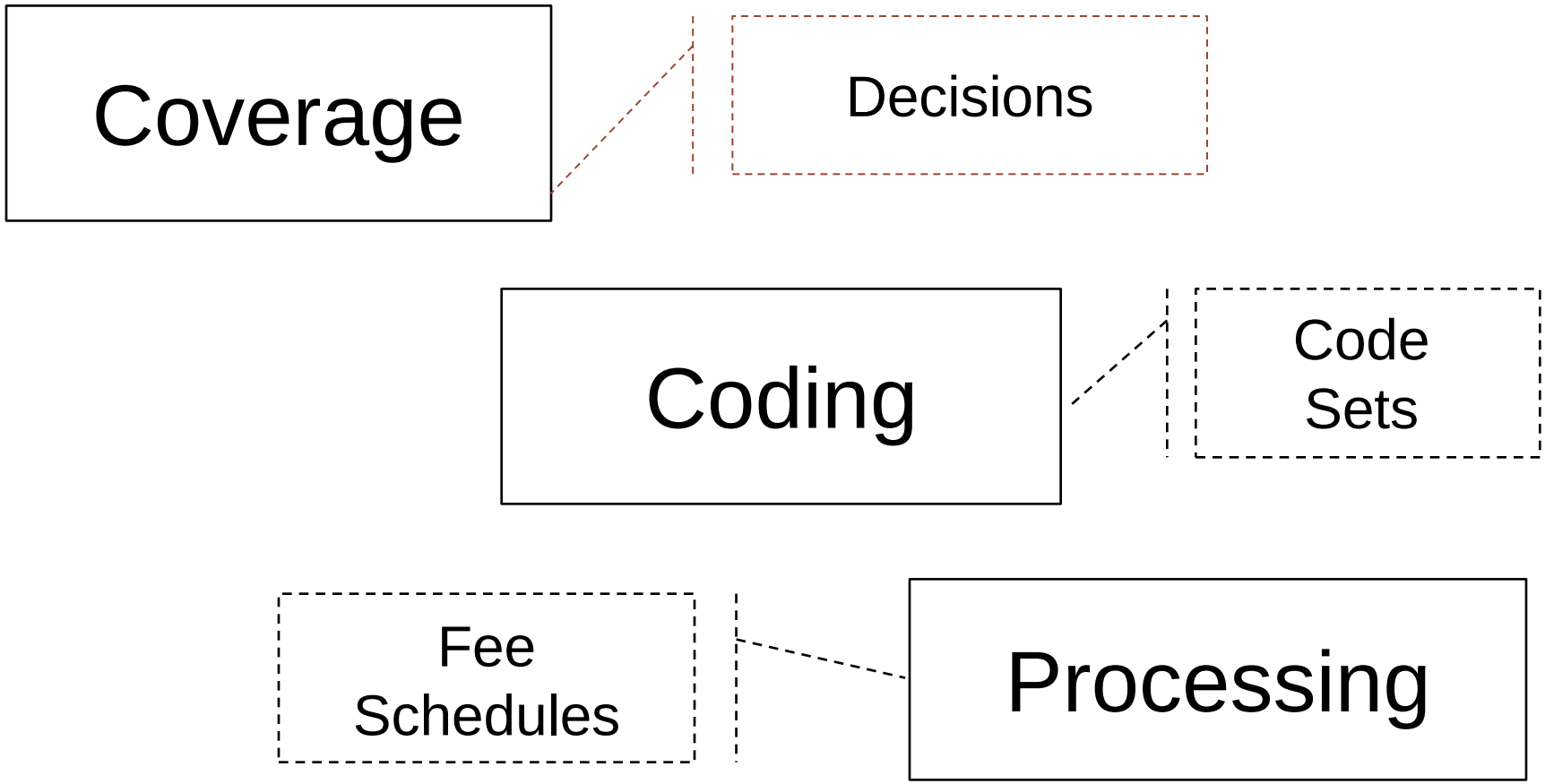
How CMS pays Medicare claims



What's in a claim?

- Information about:
  - The beneficiary,
  - The disease/condition being diagnosed/treated,
  - The provider, and
  - The service(s) provided

Processes and Files within CMS



Social Security Act §1862(a)(1)(A)

"(N)o payment may be made…for items or services – which … are not ***reasonable and necessary for the diagnosis or treatment of illness or injury*** or to improve the functioning of a malformed body member."

Definition: 'reasonable and necessary'

- Sufficient level of confidence that evidence is adequate to conclude that *the item or device improves clinically meaningful health outcomes* in Medicare beneficiaries
- CMS assesses evidence from peer-reviewed, published articles, using standard methods of evidence-based medicine (EBM)
  - Purpose: Minimize bias; reach reliable conclusions
  - E.g.: Favor studies large enough to reliably detect differences.

Evidence?

One way to define *evidence* is from a dictionary:

- "The available body of facts or information indicating whether a belief or proposition is true or valid."

Another way: examine clinical research studies

a) Findings from patient-centered clinical research on:
   1. The accuracy and precision of diagnostic tests (how good is this test?);
   2. The power of prognostic markers (does it provide good information for making clinical decisions?); and
   3. The beneficial outcomes of therapy (is the patient cured of their tumor?)

b) 'Evidence-based medicine' (EBM) is a conscientious process of obtaining and using current best evidence to make decisions about the care of individual patients.

Evidence from a Trial? What's that?

Perform a clinical trial:

- Ask a clinical question of importance and decide how best to find the answer.
- Gather the data:
  a) Divide the participants into two groups:
     1. One group gets the new treatment
     2. The other group gets the standard treatment
  b) Follow the participants until a certain amount of time has passed or a certain pre-determined outcome is reached.
- Analyze the data and publish any findings:
  a) Figure out if there's a significant difference between the two groups in a primary or secondary outcome that can be measured (e.g., survival).
  b) Publish a report about the findings of the study.

CMS is interested in outcomes such as:

- Better response to therapy
- Better health functioning (e.g., can breathe easier)
- Improved survival
- Longer symptom-free time
- Improved ability in activities of daily life
- Improved control of pain
- Other indicators of improved quality of life

CMS *doesn't* consider these as evidence:

- Testimonials
- Case reports
- Consensus reports & recommendations
- Preliminary reports (e.g., abstracts)
- Reviews in non-medical journals
- Manufacturer advertisements

Code of Federal Regulations 42 §410.32(a)

"All diagnostic x-ray and laboratory tests ***must be ordered by the physician who is treating the beneficiary … for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem.*** Tests not ordered by the physician who is treating the beneficiary are not reasonable and necessary."

CMS' Options for Coverage Policy

- When a request for new Medicare coverage is received, CMS has certain policy options:
  - CMS covers the item or service for its beneficiaries
  - CMS covers the item or service for its beneficiaries on condition that data is collected to inform future coverage policy decisions (CED)
  - CMS decides not to change existing coverage policy
  - CMS decides not to cover the item or service for its beneficiaries

- For more information on coverage, see

The Innovators' Guide to Navigating Medicare

(See final slide for website to get pdf version)

Coverage Implies Value for Clinical Use

- Example: Diagnostic testing:
  - Detection / differentiation / confirmation
  - Monitor response to therapy
  - Detect spread or recurrence
- Example: Treatment planning
  - Assess response to therapy (e.g., drug v. localized control with radiotherapy or surgery)
  - Assess anatomic relationships (e.g., volume to be treated; relation to treatment-sensitive structures or organs) for treatment planning

Coverage Determinations: Policy Statements

- National Coverage Determination (NCD) process
  1. Evidence review and analysis
  2. Proposed coverage decision

     Posted on website for public comment
  3. Final coverage decision

     Guides Medicare coverage policy nationwide
- Local Coverage Determination (LCD) process
  - Similar to national coverage process, but
    - More flexible, timely
    - Able to accommodate needs in different regions of the US

Products of the Coverage Process

1. A National Coverage Determination: our statement of national coverage policy for Medicare

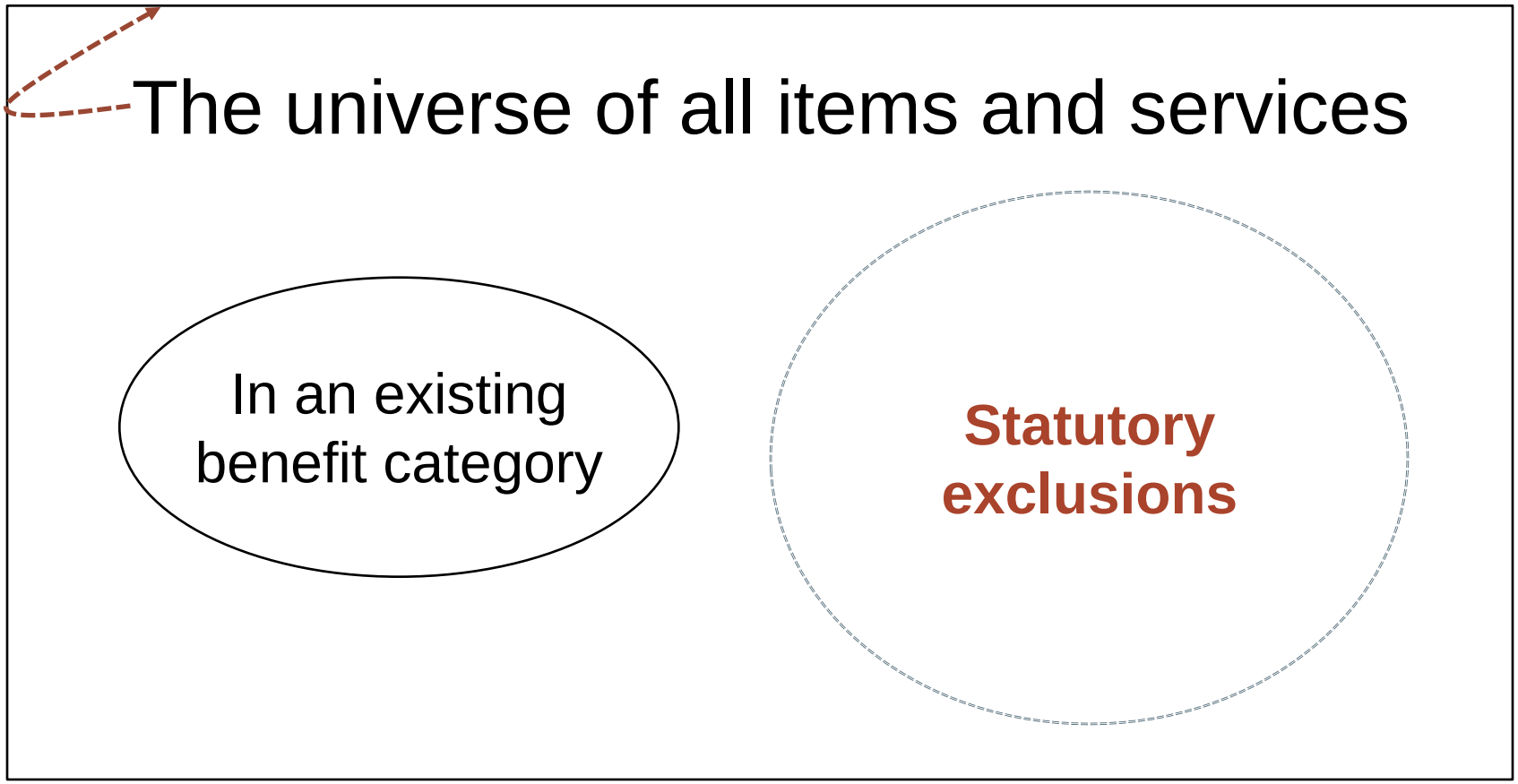
   Tracking sheet is opened to indicate that CMS is working on an NCD.

2. Opportunities for public comment
   1. When an NCD is ‘opened’ (initially posted by CMS)
   2. When a draft version of the decision memorandum has been approved within CMS

   All public comments are posted on CMS website

3. Coverage advisories to include new coverage policy within Medicare claims processing and reimbursement systems

Benefit Categories and Statutory Exclusions



Is an item/service eligible for coverage?

If it's in an existing benefit category?	If it’s statutorily excluded?
• Yes	• No
Is the correct answer	Is the correct answer

Examples of Benefit Categories

- Physicians' professional fees
- Hospital and ER charges
- Diagnostic lab / X-ray tests
- Durable medical equipment
- Preventive services benefits
  - **E.g., certain cancer screening tests**
- (and others)

Examples of Medicare Statutory Exclusions

- Hearing aids
- Eyeglasses (with exceptions)
- Routine dental care, including dentures
- Routine foot care
- Cosmetic surgery
- (and others)

CMS' top 3 questions about coverage …

Q - *Is **FDA approval or clearance** of an item or device equivalent to, or a pre-condition for, CMS coverage?*

A **NO.** The two agencies have different regulatory roles. FDA looks primarily at *safety and effectiveness*. ***In contrast***, CMS asks 'is this new item or service *reasonable and necessary* for diagnosis or treatment?' However, CMS is often guided by FDA actions regarding items or devices.

Also, CMS and FDA have announced a process, called conjoint review, allowing CMS and FDA to share information in order to accelerate the approval process for both agencies.

CMS gets questions about coverage …

Q- *May CMS consider **cost** as a factor in its coverage decisions?*

A **NO, but with an exception**: recent legislation may allow CMS in the future to consider 'expenditures' needed to obtain an item or service used in the prevention of disease (a benefit category called 'preventive service benefits'). However, this does not affect any existing preventive services benefits.

CMS gets questions about coverage …

Q - *May CMS set other criteria to regulate provider participation in the Medicare program?*

A **YES, within limits.** For example, CMS regulates clinical laboratories performing clinical diagnostic and screening services, under its CLIA statutory authority. So, even if a lab test may be covered, a lab needs to meet criteria for CLIA certification if it expects Medicare to cover that test.

Another example: CMS can affect the coding system used by providers to indicate what diagnosis they're diagnosing or treating. (Example: changeover to ICD-10-CM: 10/01/14).

(Note: 'CLIA': Clinical Laboratories Improvement Act)

Q: "*I'd like to get Medicare coverage for my new medical technology*"

Here's what you should do:

- Provide CMS with adequate evidence that
- The incremental information obtained by your new medical technology compared to alternatives
- Changes physician decisions or recommendations
- Resulting in changes in therapy or management
- That improve clinically meaningful health outcomes
- In Medicare beneficiaries.

Preferred Evidence

Useful:

- Clinical studies published in peer-reviewed medical journals, as well as
- Systematic reviews, technology assessments, statistical summaries of findings of existing studies (meta-analyses).

Not so useful:

- Abstracts; testimonials or editorials; qualitative reviews.

Assessing the value of evidence

- *More value* associated with:
  - Prospective trials
  - Controlled trials
  - Objective comparators and endpoints
  - Using techniques to reduce bias, such as randomization, masking
  - Proper use of statistical tools and well-powered studies
- *Less value* associated with:
  - Retrospective studies
  - Uncontrolled studies
  - Studies based only on self-reported survey data
  - Small studies

An example

- How does CMS approach, say, diagnostic genetic testing?
  - That is, how does CMS look at the evidence that *(in this example)* diagnostic genetic testing is reasonable and necessary, that is, it improves meaningful health outcomes for our beneficiaries?

Examining Evidence for a Genetic Test

- Analytical validity:
  - Does the genetic test accurately detect the genetic variation of interest?
- Clinical validity:
  - Do results of the genetic test accurately classify patients in ways that enable diagnostic or therapeutic decisions?
- Clinical utility:
  - Does the genetic test lead to changes in physician decisions about therapy which improve patient outcomes?

http://www.cdc.gov/genomics/gtesting/ACCE/index.htm

The National Coverage Process: More Parts

1. Medical Evidence Development and Coverage Advisory Committee Meeting (MEDCAC)
    1. Convened at CMS' option to provide guidance on evidence interpretation
    2. Includes input from topic experts, ethicists, clinical trialists, and patient representatives
    3. Open to public; transcripts are posted for public review
    4. Three MEDCAC meetings on genetic or genomic testing since 2009
2. Opportunities for public comment
    1. When an NCD is 'opened' (initially posted by CMS)
    2. When a draft version of the decision memorandum has been approved within CMS
    3. All public comments are posted on CMS website

An Example

WARFARIN RESPONSIVENESS TESTING

Melilotus officinalis / M. alba

(Photos credit: Cornell University Dept. of Animal Science)

Pictured: yellow (white) sweet clover

Karl Paul Link

(Photo Credit: Wisconsin Alumni Research Foundation)

Initial target population

(Photo credit: CDC)

Adverse Drug Event (ADE)

- Definition:
  - A healthcare encounter for a condition that the treating physician explicitly attributes to the use of a drug or a drug-specific effect.
  - "Drugs" may include prescription or over over-the counter medications; vaccines; and vitamins, dietary supplements, and herbal products.
    - "Drugs" do not include alcoholic beverages, tobacco products, and illicit substances.

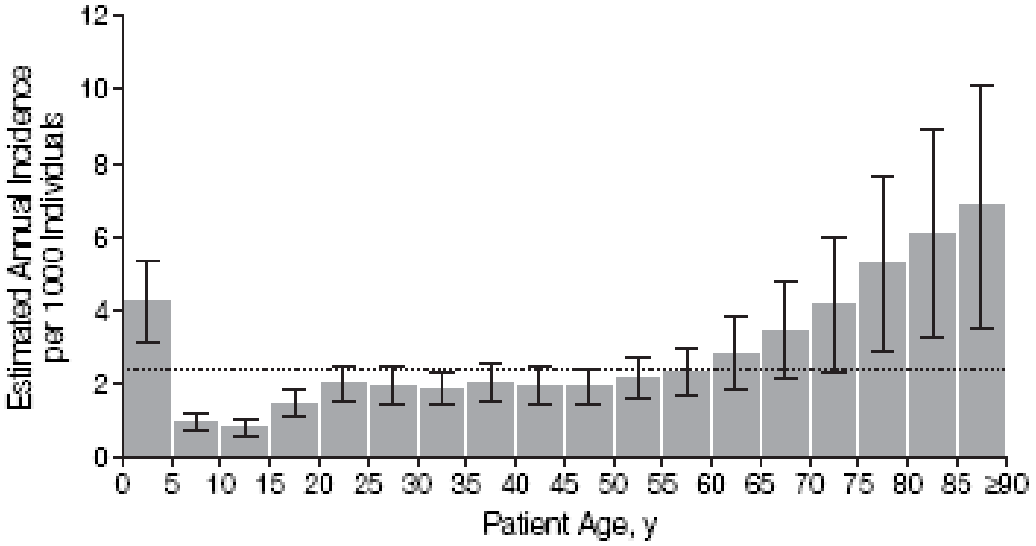
Source: DS Budnitz, Pollock DA, et al. National Surveillance of ED Visits for Outpatient ADE. JAMA 2006 Oct 18:296;1858-66

Types of ADEs

- Allergic reactions (immunologically mediated).
- Undesirable effects (either pharmacological or idiosyncratic effects at recommended doses).
- Unintentional overdoses (toxic effects linked to excess dose or impaired excretion)
  - *"ADE" does not include: intentional self-harm, therapeutic failures, drug abuse or withdrawal*.

Risk of ADEs Increases with Age

Figure. Estimated Annual Incidence of Adverse Drug Events Treated in US Emergency Departments



The estimated annual population rate of adverse drug events (dotted line) is 2.4 per 1000 (95% confidence interval, 1.7-3.0). Error bars represent 95% confidence intervals. Data are from the 2004-2005 National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance project.

DS Budnitz, Pollock DA, et al. National Surveillance of ED Visits for Outpatient ADE. JAMA 2006 Oct 18:296;1858-66

Warfarin ADEs & ED Visits

Table 5. Number of Cases and Annual Estimate of Drugs Most Commonly Implicated in Adverse Events Treated in Emergency Departments—United States, 2004-2005*

Drug	Adverse Drug Events	
	Cases, No.	Annual Estimate, No. (%)
Insulins	1577	55 819 (8.0)
Warfarin	1234	43 401 (6.2)†
Amoxicillin	1022	30 135 (4.3)
Aspirin	473	17 734 (2.5)
Trimethoprim-sulfamethoxazole	447	15 291 (2.2)
Hydrocodone-acetaminophen	420	15 512 (2.2)
Ibuprofen	526	14 852 (2.1)
Acetaminophen	497	12 832 (1.8)
Clopidogrel	241	10 931 (1.6)†
Cephalexin	293	10 628 (1.5)

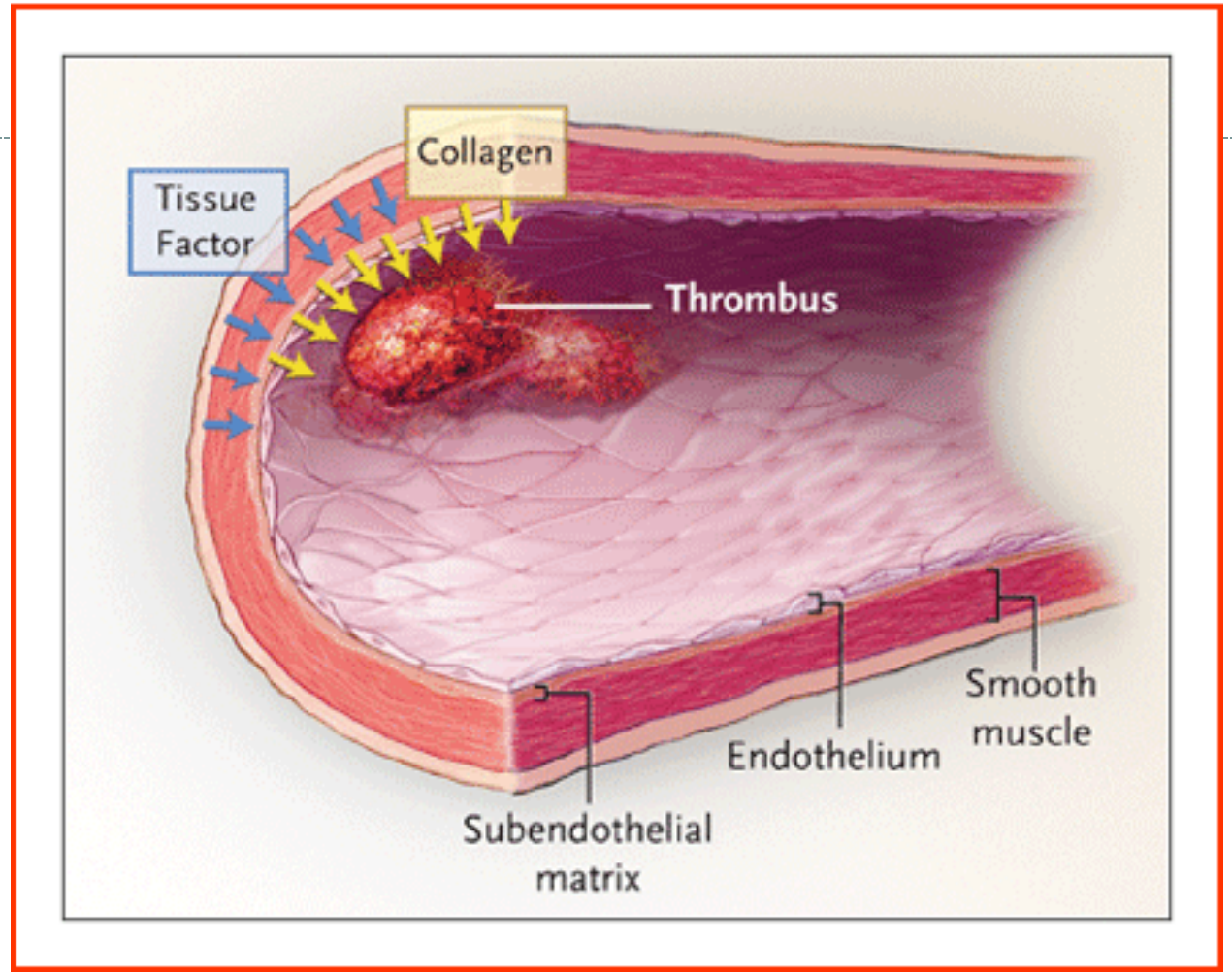
Source: DS Budnitz, Pollock DA, et al. National Surveillance of ED Visits for Outpatient ADE.

JAMA 2006 Oct 18:296;1858-66

Scope and Monitoring of Warfarin

- Per FDA, warfarin (Coumadin®) used each year by 2 million persons in U.S.
  - Difficult predicting right initial dose, esp. in elderly; modified by age, body size, other drugs taken, by consumption of certain foods
- Ways to check dose-response:
  - Prothrombin time (PT/INR)
  - **Genetic Testing (variants of *CYP2C9 & VKORC1*)**

"FDA News", August 16, 2007. "FDA Approves Updated Warfarin (Coumadin) Prescribing Information". www.fda.gov (as of 11/14/2007)



Furie B and Furie B. N Engl J Med 2008;359:938-949

Benefits: Warfarin *v*. Stroke

- " … [P]ooled data *(from multiple clinical studies)* revealed a reduction in annual stroke rate from 4.5% for the control patients to 1.4% for the patients assigned to adjusted-dose warfarin.
  - " The efficacy of warfarin was consistent across studies with an **overall relative risk reduction (RRR) of 68%** (95% confidence interval [CI], 50 to 79%).
  - " … **31 ischemic strokes will be prevented each year for every 1,000 patients treated** (or patients needed to treat [NNT] for 1 year to prevent 1 stroke = 32)."

Singer DE, Albers GW et al. Antithrombotic Therapy in Atrial Fibrillation. Chest *9/2004*

Warfarin: FDA Current Warning

WARNING: BLEEDING RISK

Warfarin sodium can cause major or fatal bleeding. Bleeding is more likely to occur during the starting period and with a higher dose (resulting in a higher INR). Risk factors for bleeding include high intensity of anticoagulation (INR >4.0), age ≥65, highly variable INRs, history of gastrointestinal bleeding, hypertension, cerebrovascular disease, serious heart disease, anemia, malignancy, trauma, renal insufficiency, concomitant drugs (see **PRECAUTIONS**) and long duration of warfarin therapy. Regular monitoring of INR should be performed on all treated patients. Those at high risk of bleeding may benefit from more frequent INR monitoring, careful dose adjustment to desired INR, and a shorter duration of therapy. Patients should be instructed about prevention measures to minimize risk of bleeding and to report immediately to physicians signs and symptoms of bleeding (see **PRECAUTIONS**: **Information for Patients**).

Source: http://www.fda.gov/cder/foi/label/2007/009218s105lblv2.pdf

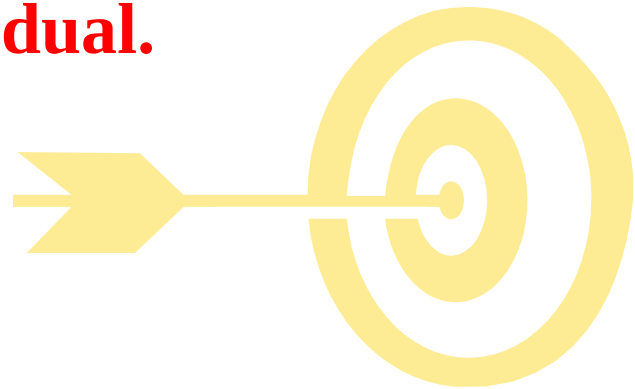
“Can’t predict ADE’s” – AHRQ, 2001

- AHRQ, in a 2001 Research Synthesis on Adverse Drug Events (ADEs) stated:
  - > 770,000 are injured or die each year
  - Cost (for hospitals): est. $ 2–6 Billions/year
  - “Anticipating who will suffer an ADE, when, and from what medication is difficult. Research has not yet identified any valid predictor of the event.”

Source: AHRQ Research Synthesis (2001) at www.ahrq.org/news/riaix.htm

Ways to Avoid ADEs

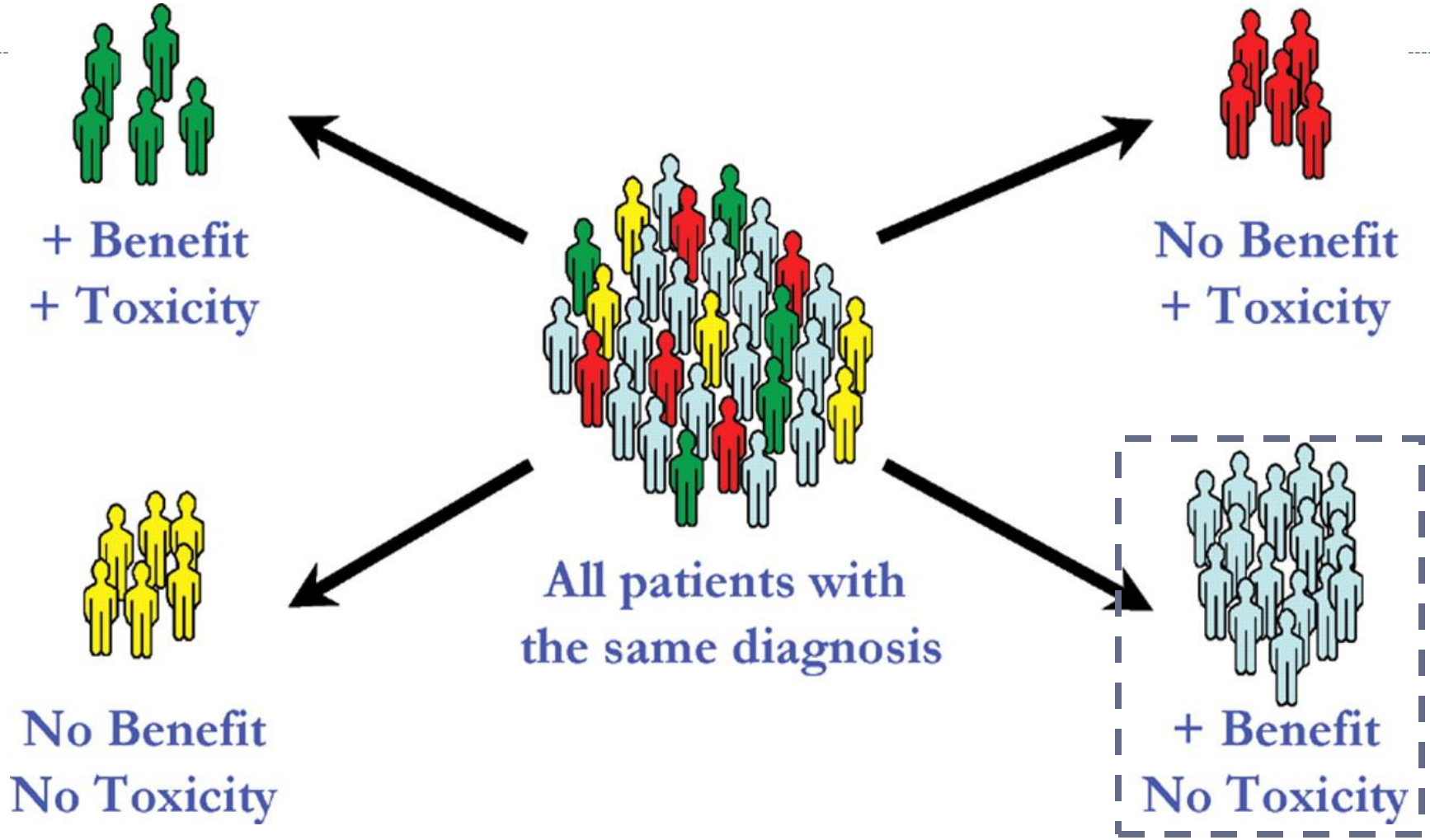
- Make sure the right patient gets the drug (e.g., improved ordering and delivery systems)
- Ensure the drug is right for that patient.
  - Select effective drug for illness or condition.
  - Choose effective dosage/route/timing.
- **Consider genetic factors which might make drug unsafe or ineffective for that individual.**



“Pharmacogenomics” (PGx)

- Around 1950, it was recognized heritable factors could affect how individuals responded to drugs (e.g., antimalarials)
  - Prior term: ‘Pharmacogenetics’
- Goal in 1990s: genetic information would allow “tailoring” of drug therapy to individual

Ideal Use of PGx Results



S. Marsh, H. McLeod. Pharmacogenomics: from bedside to clinical practice. Hum Mol Gen (2006):15, R89-93

IDEAL !

Pharmacogenomic Predictors of Adverse Reactions

Table 1. Pharmacogenomic Biomarkers as Predictors of Adverse Drug Reactions.

Gene or Allele	Relevant Drug	Specificity of Biomarker	Percent of Patients with an Adverse Reaction to Drug*
TPMT (mutant)	6-Mercaptopurines	Very good	1–10
UGT1A1*28	Irinotecan	Good	30–40
CYP2C9 and *VKORC1*	Warfarin†	Good	5–40
CYP2D6 (mutant)	Tricyclic anti-depressants	Relatively good	5–7
HLA-B*5701	Abacavir	Very good	5–8
HLA-B*1502	Carbamazepine	Very good	10
HLA-DRB1*07 and DQA1*02	Ximelagatran	Good	5–7

* Percentages are of affected whites except that for HLA-B*1502, which is the percentage of affected Asians.
† Carriage of the *CYP2C9* and *VKORC1* alleles affects warfarin dosing.

Ingelman-Sundberg M. N Engl J Med 2008;358:637-639

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Pharmacogenomic Factors Predict Drug Effect

Table 1. Pharmacogenetics of Phase I Drug Metabolism.*

Drug-Metabolizing Enzyme	Frequency of Variant Poor-Metabolism Phenotype	Representative Drugs Metabolized	Effect of Polymorphism
Cytochrome P-450 2D6 (CYP2D6)	6.8% in Sweden 1% in China[17]	Debrisoquin[15] Sparteine[16] Nortriptyline[23] Codeine[27,28]	Enhanced drug effect Enhanced drug effect Enhanced drug effect Decreased drug effect
Cytochrome P-450 2C9 (CYP2C9)	Approximately 3% in England[29] (those homozygous for the *2 and *3 alleles)	Warfarin[29,30] Phenytoin[31,32]	Enhanced drug effect[29-32]
Cytochrome P-450 2C19 (CYP2C19)	2.7% among white Americans[33] 3.3% in Sweden 14.6% in China[17] 18% in Japan[33]	Omeprazole[34,35]	Enhanced drug effect[36,37]
Dihydropyrimidine dehydrogenase	Approximately 1% of population is heterozygous[38]	Fluorouracil[39,40]	Enhanced drug effect[39,40]
Butyrylcholinesterase (pseudocholinesterase)	Approximately 1 in 3500 Europeans[41]	Succinylcholine[9,41]	Enhanced drug effect[9,41]

* Examples of genetically polymorphic phase I enzymes are listed that catalyze drug metabolism, including selected examples of drugs that have clinically relevant variations in their effects.

Weinshilboum R. N Engl J Med 2003;348:529-537

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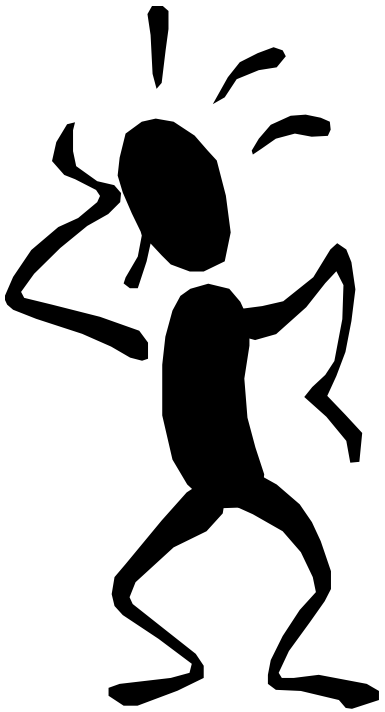
Genetics → Two Drug-Related Actions

- Genetic variants may change a target molecule, or a drug's ability to interact with it
  - Example: variants of *VKORC1* (vitamin K epoxide reductase complex 1 gene) may code for more or less response to warfarin

- Genetic variants may change how fast or slowly a drug is metabolized
  - Example: variants of *CYP2C9* (cytochrome P-450 enzyme 2C9) may more or less rapidly act on warfarin

PGx Tells if ‘Good’ DNA Has Gone ‘Bad’

- PGx can detect DNA changes that affect
  - coagulation factors themselves
  - enzymes needed for synthesis or metabolism
- PGx testing for DNA changes include
  - Single base-pair substitutions
  - Deletion of one or more nucleotides
  - [Translocation of one segment of a chromosome to a different part of that chromosome or to another chromosome (‘fusion’ genes)]
  - [Absence / duplication of chromosomes]



Questions CMS asked about genetic testing for warfarin responsiveness:

- Does published clinical evidence indicate that genetic testing improves net health outcomes for Medicare beneficiaries who are candidates for warfarin therapy?
  - Does genetic testing decrease ADEs such as over-anticoagulation and major bleeding events?
- Does published clinical evidence indicate that genetic testing improves net health outcomes for Medicare beneficiaries who are on chronic warfarin anticoagulation?
  - Does genetic testing improve survival for those on chronic warfarin therapy?

Genomic Testing for Warfarin - Timeline

Tracking sheet posted Aug. 4, 2008

- ✓ PGx NCD initiated by CMS *(CAG-00400N)*

Public Comment Period ends Sep. 3, 2008

- ✓ Dozens of comments received for CMS review

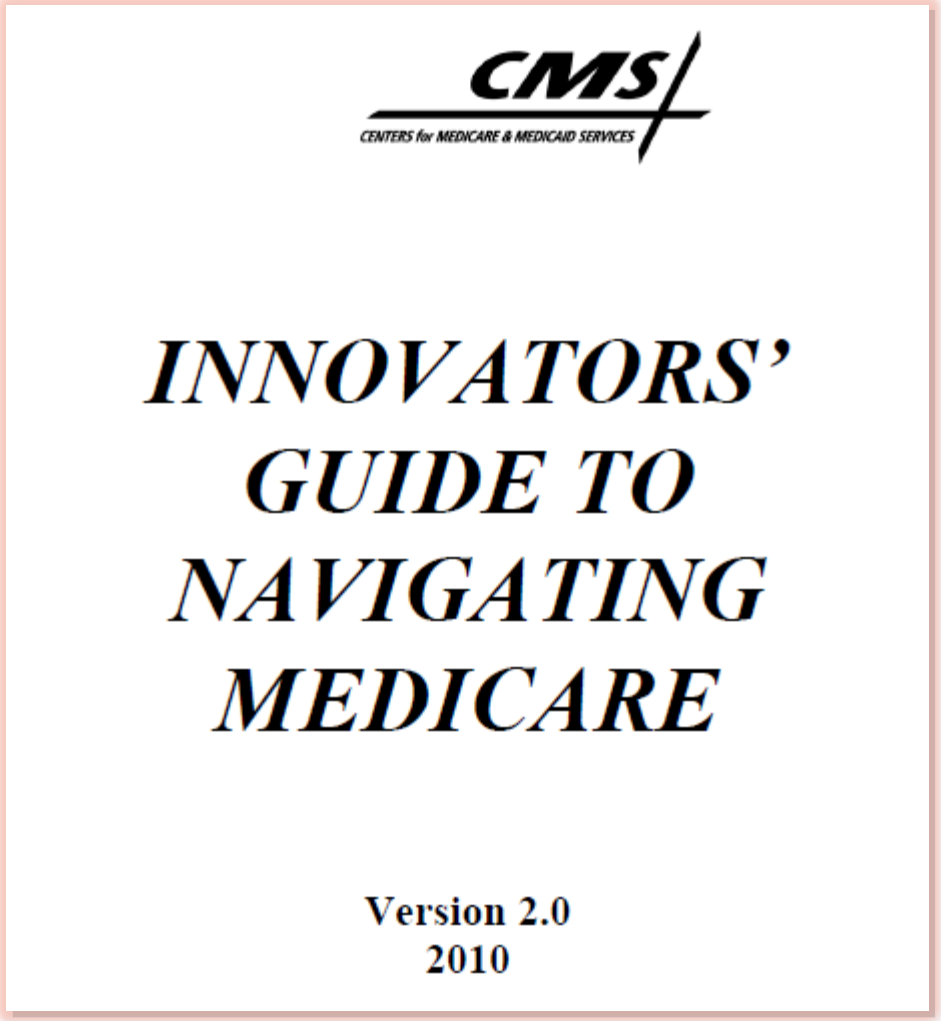
May 2009: PDM posted

- Second public comment period

August 2009: DM posted

The Book That Explains What CMS Does:

Free!



Free!

Medicare Coverage Policies for New Medical Technologies

THANKS FOR YOUR ATTENTION! ANY QUESTIONS?

[To access CMS' 'Innovators' Guide', Check the 'Downloads' section of:

http://www.cms.gov/Medicare/Coverage/CouncilonTechInnov/index.html